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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/708,006	11/08/2000	Akihiro Kishishita	197759US0CONT	1289

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1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER

ZUCKER, PAUL A

ART UNIT	PAPER NUMBER
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1621

DATE MAILED: 08/26/2003

24

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/708,006

Applicant(s)

KISHISHITA ET AL.

Examiner

Paul A. Zucker

Art Unit

1621

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 June 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____

- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Current Status

1. This action is responsive to Applicants' Request for Reconsideration of 16 June 2003 in Paper No 23.
2. Receipt and entry of Applicants' submission is acknowledged.
3. Claims 1-15 remain pending.
5. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wakamatsu et al (US 4,810,818 03-1989) and further in view of Nofre et al (US 5,480,668 01-1996).

The instantly claimed invention is a crystalline form of the Aspartame derivative Neotame, and compositions comprising it.

Wakamatsu teaches (Column 3, lines 11-43) a method of producing a more easily soluble crystalline form of aspartame which comprises granulation and drying the aspartame to a water content of 2.6% by weight. Wakamatsu further teaches (Column 2, lines 17-18) a range of granule size of 0.1 to 10 mm which embraces the instant range of 100-1,400 μm (which corresponds to 0.1-1.4 mm).

The difference between the instant invention and that taught by Wakamatsu is that Wakamatsu does not suggest the use of N-[N-(3,3-dimethylbutyl)-L- α -aspartyl]-L-phenylalanine 1-methyl ester (Neotame) in this process to create a more soluble form of neotame.

Nofre, however, teaches (Column 4, line 65-Column 5, line 10) Neotame and its synthesis (Column 6, lines 27-54) from Aspartame to which it is a close analog. Nofre further teaches (Column 1, lines 10-19) the use of Neotame as a sweetening agent in food and drinks as well as its use (Column 6, lines 16-26) in conjunction with other sweeteners such as sucrose and saccharin. Nofre further teaches (Column 6, lines 8-16) its use in conjunction with carriers or bulking agents such as polydextrose, starch, maltodextrins, and cellulose. Nofre teaches (Column 4, lines 29-37) the use of Neotame for all uses of the known sweetener aspartame.

Thus the instantly claimed invention would have been obvious to one of ordinary skill in the art. The motivation for performing this invention would have been to provide the same improved solubility for Neotame that the process of Wakamatsu provided for its close analog Aspartame, a commercially important sweetener. Because of the very close structural similarity of Neotame and Aspartame and the large overlap in their chemical and physiological behavior and intended uses the expectation for success would have been reasonable.

Examiner's Response to Applicants' Arguments with Regard to This Rejection

4. Applicants have presented several arguments with regard to this rejection. The

Examiner responds to these below:

- a. Applicants' argue (Request, page 2, 2nd full paragraph) that the Declaration of Nagashima shows that the neotame produced according to Nofre exists either in an amorphous state or as A-Type crystals. Applicants are referred to the

previous discussion in which this declaration was found deficient in Paper No 11 at paragraphs 5a and 5b.

- b. Applicants further argue that no prior art reference has been cited that stands for the proposition that the mere existence of one crystal form for a given compound suggests the existence of another different form for that compound. The Examiner agrees as pointed out by Applicants. Applicants further argue that the discovery of a new crystal form of a known compound is unexpected. The Examiner disagrees, in this instance, that the discovery of a new crystal form is surprising since Wakamatsu teaches one of ordinary skill in the art to expect that the analogues of Aspartame (of which Neotame is one) may be expected to exhibit different crystalline forms depending upon water content.
- c. Applicants further argue that the Examiner disregards the argument that different crystalline forms exhibit different physical properties which have a large influence on the industrial processing thereof. The Examiner disagrees that that he has disregarded this argument. In fact, Wakamatsu teaches this for the case of the neotame analog aspartame
- d. Applicants again argue that the discovery of a new crystal form is unexpected. The Examiner again disagrees that the discovery of a new crystal form is surprising since Wakamatsu teaches one of ordinary skill in the art to expect that the analogues of Aspartame may be expected to exhibit different crystalline forms depending upon water content. The “discovery” of

such is, in fact, expected based on the teaching of Wakamatsu. While the structure of the crystalline form may be unpredictable its existence is not.

- e. Applicants again reiterates the argument that the rejection over Wakamatsu and Nofre is deficient in that no prior art reference has been cited that stands for the proposition that the mere existence of one crystal form for a given compound suggests the existence of another different form for that compound. The Examiner again responds that such a reference is not required by the logic of the rejection and Applicants have not pointed out how it is.
 - f. Applicants further argue that the following two "assertions" by the Examiner are contradictory:
 - i. The irrelevance to the rejection that no prior art reference has been cited that stands for the proposition that the mere existence of one crystal form for a given compound suggests the existence of another different form; and
 - ii. Structural similarities between Aspartame and Neotame would have motivated the artisan to apply the methods of Wakamatsu to Neotame.
- The Examiner responds to this argument as follows:
- i. The Examiner does not see any logical nexus between i and ii above and there can therefore be no contradiction.
 - ii. Applicants have mischaracterized the Examiner's argument in ii above since structural similarities between Aspartame and Neotame are not

argued to have motivated the artisan to apply the methods of Wakamatsu to Neotame but, instead, to provide the expectation for success in applying the methods of Wakamatsu to Neotame.

- g. Applicants argue that in light of *In re Certain Cefadroxil Crystalline Monohydrate*, 15 USPQ2d 1263 (US ITC 1990) and *In re Cofer*, 148 USPQ 268 (CCPA 1966) that a new crystalline form of a compound is not obvious absent evidence that “the prior art suggests the particular structure or form of the compound or composition as well as suitable methods for obtaining that structure or form”. Applicants interpret this to mean that the specific structure of instant crystal type “C” must be suggested. The Examiner disagrees. The Examiner considers Wakamatsu’s teaching of a more stable soluble form of Aspartame (corresponding to material having the instantly desired properties) a sufficient suggestion of form.
- h. Applicants’ present (Response, page 8, top 2/3) a description of the teachings of Wakamatsu, allegedly supported by the disclosure of Sugiyama et al (US 5,479,747 04-1986), which appears to represent a conflation of the two references for which no logical support is provided. Sugiyama, however, does, in general terms, seem to support the Examiner’s position that different crystalline forms of Aspartame (and its analogue Neotame) are to be expected with varying water content.
- i. Applicants conclude on the basis of the above-noted conflation that the references teach that as water content is reduced so is solubility and that this

is in contrast to the present invention. The Examiner disagrees. Wakamatsu teaches that a more stable highly soluble form of Aspartame can be obtained by drying to water contents as low as 1.9%. Sugiyama is completely silent with regard to solubility of the different crystalline forms.

Applicant's arguments filed 16 June 2003 have been fully considered but they are not persuasive for the reasons set forth above.

Conclusion

5. Claims 1-15 are pending. Claims 1-15 are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul A. Zucker whose telephone number is 703-306-0512. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 703-308-4532. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Paul A. Zucker, Ph.D.
Patent Examiner
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